REMARKS

In response to the Office Action of June 23, 2008, Claims 1, 3-8, 11 and 14 have been amended. Claim 2 has been cancelled and its limitation incorporated in Claim 1. Amended Claim 1 is the only independent claim under consideration.

Original Claims 1, 6 and 7 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claim 1 has been amended to obviate that rejection. Claims 6 and 7 depend from Claim 1 and, accordingly, their rejections should also be obviated.

Claims 1-15 were also rejected under 35 U.S.C. § 112, second paragraph. In response thereto, the term "general" has been deleted in each instance where it occurred. Accordingly, that rejection should also be withdrawn.

Claims 11-13 were rejected under 35 U.S.C. § 103(a). Applicants respectfully request reconsideration of that rejection. In that regard, it is well known to the skilled person that trimethylsilyl group or triethylsilyl group is easily deprotected under an acidic condition. As described on page 40 of the publication Protective Groups in Organic Synthesis (John Wiley & Sons, Inc., 1981)), copy attached, even a trace of acetic acid can deprotect trimethylsilyl group or triethylsilyl group. In the EP 559533 reference, it is described that any tri-lower alkyl silyl group can be used as R1 of the compound (I). But, according to the method described in that reference, trimethylsilyl group or triethylsilyl group is easily deprotected and the compound (I) having trimethylsilyl group of triethylsilyl group as R1 cannot be obtained. That is, because thionylchloride is used as a reagent to produce the compound (I) and the obtained reaction mixture is extracted by ethylacetate and washed, trimethylsilyl group or triethylsilyl group is deprotected and it is impossible to produce the compound corresponding to the compound (3) in Claim 11 of the present application. Accordingly, a skilled person would not be able to achieve the invention of Claims 11-13 from the EP 559533 reference.

Regarding, WO 2004/035539 A1, this reference was submitted in the IDS. The Japanese language document was submitted and apparently separated from the IDS. A "copy of the actual WIPO document" has now been provided with a copy of the IDS.

The Application should now be in condition for allowance. Passage to issue is respectfully requested.

Respectfully submitted,

Attachment: 1981 Publication

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Protective Groups in Organic Synthesis

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[4] For a discussion of the use of this ether in nucleoside syntheses, see K. K. Ogilvie, S. L. Beaucage, A. L. Schifman, N. Y. Theriault, and K. L. Sadana, *Can. J. Chem.*, **56**, 2768 (1978).

[5] A. G. Mclones, *Can. J. Chem.*, **43**, 1998 (1965).

43. Trimethylsilyl Ether (TMS Ether): $ROSi(CH_3)_3$, 43

Many reagents (e.g., trimethylchlorosilane, hexamethyldisilazane, *N,O*-bistrimethylsilylacetamide, bistrimethylsilylurea, *N*-trimethylsilyl-*N,N'*-diphenylurea, trimethylsilylimidazole, trimethylsilyldiethylamine, and monotrimethylsilylacetamide) form trimethylsilyl derivatives of compounds with an active hydrogen.[a,b] Some conditions that have been used to prepare trimethylsilyl ethers are shown below.

Formation

(1) $ROH + Me_3SiCl \xrightarrow[25°,\ 8\ h,\ 90\%]{Et_3N,\ THF[c]} ROSiMe_3$

(2) $ROH + Me_3SiCl \xrightarrow[25°,\ 12\ h,\ 75\text{–}95\%]{Li_2S,\ CH_3CN[d]} ROSiMe_3$

Silylation occurs under neutral conditions with this combination of reagents.[d]

(3) $ROH + (Me_3Si)_2NH \xrightarrow[20°,\ 5\ min,\ \sim 100\%]{Me_3SiCl,\ Py[e]} ROSiMe_3$

ROH = carbohydrate

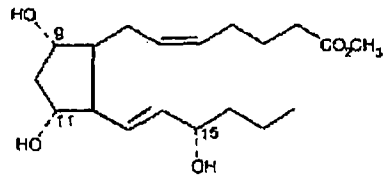
(4) $ROH + (Me_3Si)_2O \xrightarrow[reflux,\ 4\ days,\ 80\text{–}90\%]{C_5H_5\overset{+}{N}H\ OTs^-,\ C_6H_6,\ mol\ sieves[f]} ROSiMe_3$

These are only mildly acidic conditions, suitable for acid-sensitive alcohols.[f]

(5) $ROH + Me_3SiNEt_2$[g] $- ROSiMe_3$

Trimethylsilyldiethylamine selectively silylates equatorial hydroxyl groups in quantitative yield (4–10 h, 25°). The report indicated no reaction at axial hydroxyl groups.[g]

In the prostaglandin series the order of reactivity of trimethylsilyldiethylamine is $C_{11} > C_{15} >> C_9$ (no reaction). These trimethylsilyl ethers of secondary hydroxyl groups were hydrolyzed with aqueous methanol containing a trace of acetic acid.[h]



(6) $ROH + CH_3C(OSiMe_3)=NSiMe_3 \xrightarrow[78°]{DMF[i]} ROSiMe_3$

ROH = C_{14}-hydroxy steroid

N,O-Bis(trimethylsilyl)acetamide was used to protect a sterically hindered, tertiary hydroxyl group. The resulting trimethylsilyl ether, stable to a Grignard reaction, was slowly cleaved with 0.1 *N* HCl/10% aq THF, 25°.[i]

(7) $ROH + Me_3SiCH_2CO_2Et \xrightarrow[25°,\ 1\text{–}3\ h,\ 90\%]{cat.\ n\text{-}Bu_4N^+F^-[j]} ROSiMe_3$

Use of ethyl trimethylsilylacetate/tetra-*n*-butylammonium fluoride allows isolation of pure products under nonaqueous conditions. This reagent also converts aldehydes and ketones to trimethylsilyl enol ethers.[j]

(8) $ROH + Me_3SiNHCO_2SiMe_3 \xrightarrow[rapid,\ 80\text{–}95\%]{THF[k]} ROSiMe_3$

This reagent also silylates phenols and carboxyl groups.[k]

(9) $ROH + Me_3SiNHSO_2OSiMe_3 \xrightarrow[30°,\ 0.5\ h,\ 92\text{–}98\%]{CH_2Cl_2[l]} ROSiMe_3$

Higher yields of trimethylsilyl derivatives are realized by reaction of aliphatic, aromatic, and carboxylic hydroxyl groups with *N,O*-bis(trimethylsilyl) sulfamate than by reaction with *N,O*-bis(trimethylsilyl)acetamide.[l]

(10) $ROH + MeCH=C(OMe)OSiMe_3 \xrightarrow[50°,\ 30\text{–}50\ min,\ 83\text{–}99\%]{CH_3CN\ or\ CH_2Cl_2[m]} ROSiMe_3$

This reagent also silylates phenols, thiols, amides, and carboxyl groups.[m]

(11) $ROH + Me_3SiCH_2CH=CH_2 \xrightarrow[70\text{–}80°,\ 1\text{–}2\ h]{TsOH/CH_3CN[n]} ROSiMe_3,\ 90\text{–}95\%$

Formation of silyl derivatives may be effected by reaction with an allylsilane under acid catalysis. This silylating reagent is stable to moisture [Me_3SiCl and

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